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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,823	06/01/2005	Akira Kawahara	OMY-0041	7306

23353 7590 06/11/2007

RADER FISHMAN & GRAUER PLLC
LION BUILDING
1233 20TH STREET N.W., SUITE 501
WASHINGTON, DC 20036

EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
06/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,823	KAWAHARA ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 28* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 21-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/7/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/19/07 has been entered.

2. Claims 25-27 and 29 were canceled. Claims 20 and 28 have been amended. Claims 1-24 and 28 are pending in the application, with claims 1-19 and 21-24 currently withdrawn. Claims 20 and 28 are subject to examination below.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement filed 4/19/07 has been received and entered into the application. The references therein have been considered by the examiner as indicated on the attached form PTO-1449.

Objections/Rejections Withdrawn

4. The objections to claims 28-29 have been withdrawn in response to the amendments to claim 28 and in light of the cancellation of claim 29.

5. The rejections under 112, 2nd paragraph have been obviated by the amendments.

Specification

6. The amendment filed 9/21/06 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

On p. 33, line 17 of the marked-up copy of the substitute specification the words "polyclonal antibody" have been changed to "antigen". This changes the meaning of the passage since an antigen is a distinct molecule from a polyclonal antibody.

On p. 35, line 3 of the marked-up copy of the substitute specification the words "Anti-VTG antibody" have been changed to "VTG antigen". This change represents new matter because as originally filed, the specification disclosed an **antibody** coupled to Sepharose, while the specification as amended discloses an **antigen** coupled to Sepharose.

The changes are deemed to represent new matter since antibodies and antigens cannot be considered to be interchangeable terms, and Applicant has not established that the amendments represent correction of an obvious error (see MPEP 2163). Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 20 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawahara et al. ("Quantitative analysis of protein synthesis altered by estrogen in cultured *Xenopus* liver parenchymal cell" (1981) Develop., Growth and Differ. 23, 599-611) in view of Dunbar et al. ("Preparation of Polyclonal Antibodies" (1990) *Methods in Enzymology* **182**, 663-670) and Harlow & Lane ("Antibodies: A Laboratory Manual" (1988) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pages 283, 285-295, 302-303 and 313). The Kawahara et al. and Dunbar et al. references are already of record; the Harlow & Lane has been amended to include additional pages not previously relied upon.

Kawahara et al. teach polyclonal antisera specific for frog (*Xenopus laevis*) vitellogenin, which was collected from immunized rabbits (see the entire document, especially the abstract and p. 601, "Immunological identification of vitellogenin").

Regarding the recitation that the polyclonal antibody is prepared by "purifying the IgG by an adsorption purification column coupled with blood serum proteins of a male frog", it is noted that this limitation has been interpreted as reasonably conveying that the polyclonal antibody would not significantly cross-react with male frog blood serum proteins.

The Kawahara et al. reference teaches that the prepared antisera were absorbed with normal male sera in order to obtain vitellogenin-specific antisera. Thus, the reference clearly teaches that the antibody produced was specific for vitellogenin and not for other proteins in normal male sera. Although the reference fails to specifically mention in the brief experimental section that the adsorption process involved a "column", it reads on the claim because in product-by-process claims, a determination of patentability is based on the product itself, and not on the limitations of the steps recited. See MPEP 2113. In the instant case, since the crude antisera of Kawahara et al. were adsorbed against male frog sera (and proteins therein) to result in *vitellogenin-specific antisera*, the reference clearly teaches a product that has specificity for vitellogenin and not for other male frog serum proteins.

The recitation of a "column" fails to further limit the claimed product because no additional structural difference are implied in the resulting polyclonal antibodies, beyond that already implied by the reference to adsorption purification against blood serum proteins of a male frog (which connotes that the resulting polyclonal antibodies would be specific for vitellogenin and not for other male frog proteins). As such, although Kawahara et al. fail to specifically mention that a "column" was used for the adsorption purification step, the antibody produced by the process detailed in the reference appears to be similar since no structural differences are implied through the use of a "column" vs. a process where the antibody is adsorbed to male serum proteins by a "batch" method, for example.

With respect to the recitation that the polyclonal antibody is prepared by "isolating IgG fraction," this limitation has been interpreted as reasonably conveying that the claimed

polyclonal antibody would be an IgG fraction. Kawahara et al. fail to specifically teach isolation of the IgG fraction.

Regarding the limitation of "purifying the IgG by...any affinity purification column coupled with a frog vitellogenin", this limitation has been considered in terms of the structure implied by the process of affinity purification in light of the data presented in the specification at Figure 18, where it is seen that specific antibody titers increase after affinity purification. Kawahara et al. fail to specifically teach a polyclonal antibody produced by such an affinity purification process.

Dunbar et al. teach that it is often desirable to partially purify polyclonal antibodies from antiserum prior to use (p. 669-670, "Fractionation of Ig from Serum"). In particular, Dunbar et al. teach DEAE-Sephacel ion-exchange chromatography as well as protein A affinity chromatography as methods to yield the IgG fraction, purified from other immunoglobulin subclasses and most serum proteins (page 669). It is noted that DEAE chromatography is also one of the methods disclosed in the instant specification for the purpose of isolating the IgG fraction (page 30).

Harlow & Lane teach methods of purifying antibodies, and in particular polyclonal antibodies (see especially Table 8.4). The reference teaches a purification scheme involving ammonium sulfate fractionation in combination with DEAE for obtaining the IgG fraction (Table 8.4) , which is the same method disclosed by Dunbar et al. above and also in the instant specification (page 30). The reference also teaches other purification steps that result in purification of the IgG fraction, such as caprylic acid in combination with ammonium sulfate.

Thus, like Dunbar et al. above, Harlow & Lane establish that it was well known in the art to obtain the IgG fraction of polyclonal antibodies for the purpose of purification.

Harlow & Lane further teach affinity purification methods involving an antigen affinity column, in which the antigen is bound covalently to a solid support. Such methods can be used for producing highly pure and specific polyclonal antibodies (Table 8.4, p. 293 and 313). The reference further teaches that affinity purification on an antigen column has a unique ability to isolate specific antibodies from a mixed pool (Tables 8.3-8.4; pages 288-290 and 313).

Harlow & Lane teaches that purified antibodies are desirable for a number of reasons, in that they may lower the background in some assays (p. 288). Also, when labeled antibodies are used to detect antigens directly, the antibodies must be purified first. It is also noted that the examiner took official notice in the previous Office action that the benefit of using purified reagents was well known in the art (see the Office action mailed 10/19/06). Because applicant has not traversed the examiner's assertion of official notice the well-known in the art statement is taken to be admitted prior art. See MPEP 2144.03.

Harlow & Lane also teaches that it is often necessary to combine several purification methods in order to achieve the desired purification (page 289).

Therefore, it would have been obvious to one of ordinary skill in the art to isolate the IgG fraction of the polyclonal antibody of Kawahara et al. from antiserum as taught by either Dunbar et al. or Harlow & Lane because the references teach that such a step is effective in purifying polyclonal antibodies and that such purification is desirable prior to using the antibodies. One would be motivated to employ IgG-fractionated polyclonal antibodies for the clear benefit of

having more pure reagents, e.g. in lowering background for use in assays or when labeled reagents are needed.

It would have been further obvious to one of ordinary skill in the art at the time of the invention to also include a step of purifying the polyclonal antibodies on an antigen (i.e. vitellogenin) affinity column in order to obtain a highly pure and specific preparation. In particular, given that both IgG fractionation and affinity chromatography on an antigen column were recognized in the prior art to be methods of purifying polyclonal antibodies, it would have been obvious to perform such methods together for the sample purpose, namely in order to obtain antibodies of higher purity. See MPEP 2144.06.

Furthermore, in light of the teachings of Harlow & Lane that it is often necessary to combine several purification methods in order to achieve desired purification of an antibody, it would have been obvious to combine together the multiple purification methods taught in the prior art.

With respect to the order in which the purification steps are performed in the claimed invention, Applicant is reminded that the selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.). See MPEP 2144.04. As such, it would have been obvious to one of ordinary skill in the art to select any order of the purification steps in order to achieve the desired result of purification with a reasonable expectation of success.

With respect to claim 28, Applicant has not provided evidence to establish that polyclonal antibodies elicited against vitellogenin induced in a *male* frog would be structurally different

than polyclonal antibodies elicited against vitellogenin induced in a *female* frog as in Kawahara et al. Since no structural differences are clearly implied as a result of the recited process step, the claimed product appears to be the same or similar to that of the prior art. See MPEP 2113.

10. Claims 20 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. ("*In Vitro* Translation and Estradiol-17β Induction of *Xenopus laevis* Vitellogenin Messenger RNA" *The Journal of Biological Chemistry* Vol. 251 No. 10, p. 3105-3111, 1976) in view of Kawahara et al. and Harlow & Lane ("Antibodies: A Laboratory Manual" (1988) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pages 283, 285-295, 302-303 and 313).

See the rejection above for further elaboration regarding claim interpretation.

Shapiro et al. teach polyclonal antibodies specific for frog (*Xenopus laevis*) vitellogenin (see especially the abstract and p. 3105-3106, "Methods" and p. 3106, right column, "Characterization of Antibodies"). Although the reference does not use the term "polyclonal" to describe the antibodies, the process set forth in the reference would be immediately envisaged by one skilled in the art as one producing polyclonal, rather than monoclonal, antibodies. The reference teaches that the antibodies were produced by immunizing rabbits with purified vitellogenin and isolating the antisera (see in particular p. 3106, the left column). The reference further teaches preparing the IgG (γ-globulin) fraction by ammonium sulfate fractionation (p. 3106, "Preparation of Antibodies").

Shapiro et al. fail to specifically teach that the polyclonal antibodies were additionally purified by adsorption and affinity purification.

Kawahara et al. (discussed in detail above), teach production of polyclonal antibodies against vitellogenin, in which the prepared antibodies are subsequently absorbed with normal male frog serum in order to obtain antibodies specific for vitellogenin (p. 601, "Immunological identification of vitellogenin").

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to adsorb normal male frog serum (and therefore the proteins contained therein) with the polyclonal antibody preparation of Shapiro et al. in order to isolate those antibodies in the preparation that are *specific for vitellogenin*, as taught by Kawahara et al. One would be motivated to do this in order to obtain antibodies specific for vitellogenin, which are useful in assays for detecting this protein. The use of a "column" during the adsorption process is not found to further limit the patentability of the claimed product, as discussed further above.

Harlow & Lane (discussed above) teach methods of purifying antibodies, including ammonium sulfate fractionation as well as affinity purification on an antigen column (see especially Tables 8.3-8.4; pages 288-290 and 313). Such affinity purification methods using an antigen affinity column, in which the antigen is bound covalently to a solid support, can be used for producing highly pure and specific polyclonal antibodies (p. 293 and 313). The reference further teaches that affinity purification on an antigen column has a unique ability to isolate specific antibodies from a mixed pool.

The reference also teaches that purified antibodies are desirable for a number of reasons, in that they may lower the background in some assays (p. 288). Also, when labeled antibodies are used to detect antigens directly, the antibodies must be purified first. The reference teaches

that ammonium sulfate fractionation alone is not recommended as a single step, since it still yields impure antibody, and that it must be coupled with other techniques (Table 8.3 at p. 292).

Therefore, it would have been further obvious to one of ordinary skill in the art at the time of the invention to purify the polyclonal antibodies of Shapiro et al. and Kawahara et al. on an antigen (i.e. vitellogenin) affinity column in order to obtain a highly pure and specific preparation, as taught by Harlow & Lane, since ammonium sulfate fractionation alone (as was done in Shapiro et al.) is not recommended as a single step for purifying antibodies, but must be coupled with other purification techniques. As such, it would have been obvious to include other known methods for the same purpose of purification given the clear direction of Harlow & Lane that it is often necessary to combine several purification methods in order to achieve desired purification of an antibody.

With respect to the order in which the purification steps are performed in the claimed invention, Applicant is reminded that the selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.). See MPEP 2144.04. As such, it would have been obvious to one of ordinary skill in the art to select any order of the purification steps in order to achieve the desired result of purification with a reasonable expectation of success.

With respect to claim 28, Shapiro et al. teach that the antibodies were produced using vitellogenin antigen produced in male frogs induced with estradiol-17β (p. 3105-3106). Since this vitellogenin preparation served as the antigen in raising the antibody of Shapiro et al., it would have been further obvious to also employ this same preparation as the antigen in the

antigen affinity column taught by Harlow & Lane, since Harlow & Lane directs the skilled artisan to couple corresponding antigens for an antibody to a solid support to obtain highly pure preparations of the antibody in this fashion.

Response to Arguments

11. With respect to the objections to the substitute specification filed 9/21/06 as containing new matter, Applicant argues (see page 7) that the changes were made to correct errors in translation of the original Japanese text, JP 2002-167920. Applicant's arguments have been fully considered but they are not persuasive.

MPEP 2163.06 states that:

> [w]here a U.S. application as originally filed was in a non-English language and an English translation thereof was subsequently submitted pursuant to 37 CFR 1.52(d), if there is an error in the English translation, applicant may rely on the disclosure of the originally filed non-English language U.S. application to support correction of an error in the English translation document.

However, in the instant case Applicant is attempting to rely not on the originally filed PCT application but on the foreign priority document, JP 2002-167920. Although a portion of a foreign priority application may be entered into the U.S. application to permit the correction of translation error in the U.S. application where the foreign priority application is in a non-English language, this is only permissible in situations where the foreign priority application has been properly incorporated by reference. See MPEP 201.13, section II-G, and MPEP 608.01(p).

Since an explicit incorporation by reference statement to the prior-filed foreign priority application was not made at the time of filing, Applicant is not entitled to rely on the content of the foreign priority document to correct errors in translation.

12. With respect to the rejection of claims 20 and 28 under 35 USC 103(a) as being unpatentable over Kawahara et al. in view of Dunbar et al. and Harlow & Lane, Applicant's arguments (see pages 8-13) have been fully considered but are not persuasive.

13. Applicant argues that the adsorption purification step described in Kawahara, because the reference does not specifically mention a "column", would result in "[a]ntibody neutralized with frog blood serum proteins will remain in vitellogenin specific anti blood serum obtained by adsorption purification which does not use a column" (see page 9). This is not found persuasive because Kawahara et al. clearly teach that "[t]he prepared antisera were absorbed with normal male sera in order to obtain vitellogenin specific antisera; their specificity against vitellogenin was tested". Thus, the evidence of record reflects that the adsorption purification method described by Kawahara et al. produced *vitellogenin-specific* antibodies.

Applicant's arguments that somehow the purification process of Kawahara et al. did not in fact result in separation of those antibodies adsorbed or neutralized from those vitellogen-specific antibodies is unsupported by any evidence of record, and is contrary to the evidence of record as taught in the reference itself.

The fact that Kawahara et al. fail to specifically mention the use of a "column" does not detract from the relevant teaching that polyclonal vitellogenin-specific antibodies were produced by absorption purification against normal male sera. As such, even if Kawahara et al. did not use a "column" during this process, Applicant has not established that any structural differences would accrue to the resulting polyclonal antibody as compared to an antibody produced by adsorption purification performed by a "batch" method, for example. See for example Harlow &

Lane (discussed above), which teaches that purification steps need not include a column in order to achieve separation or purification, but rather can be performed in "batch" (pages 302-303).

Adsorption against male sera and subsequent obtaining of the vitellogenin-specific antisera, whether performed in a column or not, would have the same effect of selecting for those antibodies that bind to vitellogenin, such as those taught by Kawahara et al. As such, the recitation of a "column" adds nothing further to the claim and is not found to further limit the claimed product.

14. In response to applicant's arguments against the references individually (see page 9, the second full paragraph, to page 10, the first full paragraph; and also the paragraph bridging pages 12-13), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

15. With respect to the order in which the adsorption purification and the affinity purification steps are performed in the claimed invention, Applicant argues that it is not obvious to produce products equivalent to those claimed by combining the steps taught in the references or to designate the order of process steps (see Applicant's reply, pages 11-12 and the "Appendix" of pages 14-17).

To support this Argument, Applicant has provided experimental data attached as an "Appendix". It appears that such data have been offered to attest to unexpected results.

Initially, it is noted that the "Appendix" has not been supplied in Declaration or Affidavit Form. As such, it is difficult to fully evaluate the weight of such statements made therein as to their probative value. The reason for requiring evidence in declaration or affidavit form is to

obtain the assurances that any statements or representations made are correct, as provided by 35 U.S.C. 25 and 18 U.S.C. 1001. See MPEP 716.02(g).

Applicant is reminded that the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are *not evidence* and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, as in the instant case. See MPEP 706.01(c).

In particular, Applicant argues that by first performing adsorption purification followed by affinity purification, the resulting antibody is different in quality (Reply, page 11).
It is unclear who performed such experiments and who is attesting to the data, since the Appendix has not been supplied in Declaration or Affidavit form.

The data presented in the Appendix describe experiments made involving a first antibody ("Antibody 1") that was first adsorbed and then affinity purified and a second antibody ("Antibody 2") that was first affinity purified and then adsorbed (see page 14). The author of the Appendix concludes that Antibody 1 is 30-fold higher in specificity than Antibody 2.

However, even when such data are considered, they fail to outweigh the evidence of obviousness, for the following reasons.

The claims are drawn to a polyclonal antibody specific for frog vitellogenin. The data presented in the Appendix refer only to an "antibody", but do not specify whether the antibody is polyclonal. As such, the experiment reported does not represent a depiction of the claimed invention and is not commensurate in scope with the claims. In addition, the claims fail to recite

any limitations pertaining to the "sensitivity" of the claimed antibody, and therefore fail to distinguish over the prior art on any such basis.

Furthermore, whether evidence shows unexpected results is a question of fact and the party asserting unexpected results has the burden of proving that the results are unexpected. In re Geisler, 116 F.3d 1465, 1469-70, 43 USPQ2d 1362, 1364-5 (Fed. Cir. 1997). It is not enough to merely establish a difference in results – the results must be shown to be unexpected to a person having ordinary skill in the art. In re Harris, 409 F.3d 1339, 1344, 74 USPQ2d 1951, 1955 (Fed. Cir. 2005)("The 32-43% increase in stress-rupture life, however, does not represent a 'difference in kind' that is required to show unexpected results.")(citing In re Huang, 100 F.3d 135, 139, 40 USPQ2d 1685, 1688 (Fed. Cir. 1989)).

In the instant case, the data purport to show a *difference* in sensitivity, but Applicant has not established that such a difference is *unexpected.* In addition, the attested 30-fold difference in sensitivity at best represents a *difference in degree*, rather than a *difference in kind.*

For all of these reasons, Applicant's arguments and the data presented therein fail to outweigh the evidence of obviousness.

16. With respect to the rejection of **claim 28** as being unpatentable over Kawahara et al. in view of Dunbar et al. and Harlow & Lane, Applicant's arguments (see page 11) have been fully considered but are not persuasive. Although product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. In the instant case, no structure implied by the process steps recited in claim 28 is readily apparent. Because the claimed product appears to be the same or similar to that of the prior art, although produced

by a different process, the burden is on applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. See MPEP 2113.

In the instant case, Applicant argues in effect that "there is a possibility" that antibody raised against vitellogenin from a female frog may differ from antibody raised against a male frog (page 11). Such arguments that the antibodies *might differ* as a result of the recited process step fail to establish an unobvious difference, particularly as the arguments of counsel cannot take the place of evidence in the record. Applicant has not provided any documentation or evidence to support such possible differences in antigenicity. Moreover, the claims fail to recite any limitations pertaining to the antigenicity of the claimed antibody.

For these reasons, Applicant has not met the burden of establishing an unobvious difference between the claimed polyclonal antibody produced by a process involving frog vitellogenin that is purified by chromatography from blood serum of a male frog in which vitellogenin synthesis is induced, and the antibody of the prior art.

17. With respect to the rejection of claims 20 and 28 under 35 USC 103(a) as being unpatentable over Shapiro et al. in view of Kawahara et al. and Harlow & Lane, Applicant's arguments (see pages 8 and 11-13) have been fully considered but are not persuasive.

Applicant argues (see pages 8 and 12) that it is not obvious to determine the combination of purification steps taught in the prior art or to designate the order of such steps, which is not persuasive as discussed above with respect to Kawahara et al., Dunbar et al., and Harlow & Lane.

Applicant's arguments (see pages 11-13) regarding the lack of an explicit teaching of a "column" in Kawahara et al. are addressed above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CFoster

Christine Foster, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 06/07/07
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600